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What is claimed is:

- 10 1. A method of inhibiting activation by CD40 ligand of cells bearing CD40 on the cell surface, other than B cells, comprising contacting the cells with an agent capable of inhibiting interaction between CD40 ligand and the cells, in an amount effective to inhibit activation of the cells.
- 15 2. The method of claim 1, wherein the CD40-bearing cells are selected from the group consisting of fibroblasts, endothelial cells, epithelial cells, T cells, basophils, macrophages, Reed-Steinberg cells, and dendritic cells.
- 20 3. The method of claim 2, wherein the epithelial cells are keratinocytes.
- 25 4. The method of claim 1, wherein the agent inhibits binding of CD40 ligand to CD40 on the cells.
5. The method of claim 1, wherein the agent is a protein.
- 30 6. The method of claim 5, wherein the protein comprises an antibody or portion thereof.
7. The method of claim 6, wherein the antibody is a monoclonal antibody.
- 35 8. The method of claim 7, wherein the monoclonal antibody is a chimeric antibody.
- 40 9. The method of claim 7, wherein the monoclonal antibody is a humanized antibody.

- 5 10. The method of claim 7, wherein the monoclonal antibody is a primatized antibody.
11. The method of claim 6, wherein the portion of the antibody comprises a complementarity determining region or variable region of a light or heavy chain.
- 10 12. The method of claim 6, wherein the portion of the antibody comprises a complementarity determining region or a variable region.
- 15 13. The method of claim 12, wherein the portion of the antibody comprises a Fab, or a single chain antibody.
- 20 14. The method of claim 5, wherein the protein comprises soluble extracellular region of CD40 ligand, or variants thereof including conservative substituents, or portion thereof; or soluble extracellular region of CD40, or variants thereof including conservative substituents, or portion thereof.
- 25 15. The method of claim 14, wherein the soluble extracellular region of CD40 ligand or CD40 is a monomer.
- 30 16. The method of claim 14, wherein the soluble extracellular region of CD40 is an oligomer.
- 35 17. The method of claim 14, wherein the protein comprising soluble extracellular region of CD40 or portion thereof further comprises an Fc region fused to the extracellular region of CD40 or portion thereof.
- 40 18. The method of claim 17, wherein the Fc region is

- 5       capable of binding to protein A or protein G.
19.   The method of claim 17, wherein the Fc region  
      comprises IgG, IgA, IgM, IgD, or IgE, or subclasses  
      thereof.
- 10       20   The method of claim 19, wherein:  
              the IgG is IgG<sub>1</sub>, IgG<sub>2</sub>, IgG<sub>3</sub>, or IgG<sub>4</sub>; or  
              the IgA is IgA<sub>1</sub> or IgA<sub>2</sub>.
- 15       21.   The method of claim 1, wherein the agent  
              specifically binds to the antigen to which  
              monoclonal antibody 5c8 (ATCC Accession No. HB  
              10916) specifically binds.
- 20       22.   The method of claim 21, wherein the agent is an  
              antibody.
23.   The method of claim 22, wherein the antibody is  
      monoclonal antibody 5c8 (ATCC Accession No. HB  
25       10916).
24.   The method of claim 1, wherein the agent is a small  
      molecule.
- 30       25.   The method of claim 1, wherein the agent  
              specifically binds to CD40 on the cell surface.
26.   The method of claim 25, wherein the agent is a  
      protein.
- 35       27.   The method of claim 26, wherein the protein is an  
              antibody.
28.   The method of claim 27, wherein the antibody is a  
40       monoclonal antibody.

- 5 29. The method of claim 28, wherein the monoclonal antibody is chimeric, humanized, or primatized.
30. The method of claim 26, wherein the protein comprises the extracellular region of CD40 ligand.
- 10 31. The method of claim 1, wherein the agent is nonprotein.
32. The method of claim 1, wherein the agent is selected from a library of known agents.
- 15 33. The method of claim 1, wherein the agent is modified from a known agent.
- 20 34. The method of claim 33, wherein the modified agent is designed by structure optimization of a lead inhibitory agent based on a three-dimensional structure of a complex of soluble extracellular region of CD40 ligand or portion thereof with the lead inhibitory agent.
- 25 35. The method of claim 1, wherein the agent is selected by a screening method, which comprises:
- 30 isolating a sample of cells;
- culturing the sample under conditions permitting activation of CD40-bearing cells;
- 35 contacting the sample with cells expressing a protein which is specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 10916, or with a protein which is specifically recognized by
- 40 monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 10916, effective to

5        activate the CD40-bearing cells;

         contacting the sample with an amount of the agent  
         effective to inhibit activation of the CD40-bearing  
10        cells if the agent is capable of inhibiting  
         activation of the CD40-bearing cells; and

         determining whether the cells expressing the protein  
         which is specifically recognized by monoclonal  
15        antibody 5c8 produced by the hybridoma having ATCC  
         Accession No. HB 10916, or with the protein which is  
         specifically recognized by monoclonal antibody 5c8  
         produced by the hybridoma having ATCC Accession No.  
         HB 10916, activate the CD40-bearing cells in the  
20        presence of the agent.

36.    The method of claim 35, wherein the agent is  
         selected from a library of known agents.

25    37.    The method of claim 36, wherein the known agents are  
         nonprotein agents.

38.    A method of inhibiting activation by CD40 ligand of  
         cells bearing CD40 on the cell surface, other than  
30        B cells, in a subject, comprising administering to  
         the subject an agent capable of inhibiting  
         interaction between CD40 ligand and the cells, in an  
         amount effective to inhibit activation of the cells  
         in the subject.

35        39.    The method of claim 38, wherein the CD40-bearing  
         cells are selected from the group consisting of  
         fibroblasts, endothelial cells, epithelial cells, T  
         cells, basophils, macrophages, Reed-Steinberg cells,  
40        and dendritic cells.

- 5 40. The method of claim 39, wherein the epithelial cells are keratinocytes.
41. The method of claim 38, wherein the agent inhibits binding of CD40 ligand to CD40 on the cells.
- 10 42. The method of claim 38, wherein the agent is a protein.
43. The method of claim 42, wherein the protein comprises an antibody or portion thereof.
- 15 44. The method of claim 43, wherein the antibody is a monoclonal antibody.
- 20 45. The method of claim 43, wherein the monoclonal antibody is a chimeric antibody.
46. The method of claim 44, wherein the monoclonal antibody is a humanized antibody.
- 25 47. The method of claim 44, wherein the monoclonal antibody is a primatized antibody.
48. The method of claim 43, wherein the portion of the antibody comprises a complementarity determining region or variable region of a light or heavy chain.
- 30 49. The method of claim 43, wherein the portion of the antibody comprises a complementarity determining region or a variable region.
- 35 50. The method of claim 49, wherein the portion of the antibody comprises a Fab, or a single chain antibody.
- 40 51. The method of claim 38, wherein the agent

- 5 specifically binds to the antigen to which  
monoclonal antibody 5c8 (ATCC Accession No. HB  
10916) specifically binds.
- 10 52 The method of claim 51, wherein the agent is an  
antibody.
53. The method of claim 52, wherein the antibody is  
monoclonal antibody 5c8 (ATCC Accession No. HB  
10916).
- 15 54. The method of claim 38, wherein the subject is a  
mammal.
- 20 55. The method of claim 54, wherein the mammalian  
subject is a human.
56. The method of claim 54, wherein the mammalian  
subject is a rodent.
- 25 57. The method of claim 38, wherein the protein  
comprises soluble extracellular region of CD40  
ligand, or variants thereof including conservative  
substituents, or portion thereof; or soluble  
extracellular region of CD40, or variants thereof  
30 including conservative substituents, or portion  
thereof.
58. The method of claim 57, wherein the soluble  
extracellular region of CD40 ligand or CD40 is a  
35 monomer.
59. The method of claim 57, wherein the soluble  
extracellular region of CD40 is an oligomer.
- 40 60. The method of claim 57, wherein the protein  
comprising soluble extracellular region of CD40 or

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- 5 portion thereof further comprises an Fc region fused  
to the extracellular region of CD40 or portion  
thereof.
- 10 61. The method of claim 60, wherein the Fc region is  
capable of binding to protein A or protein G.
62. The method of claim 60, wherein the Fc region  
comprises IgG, IgA, IgM, IgD, or IgE, or subclasses  
thereof.
- 15 63. The method of claim 62, wherein:  
the IgG is IgG<sub>1</sub>, IgG<sub>2</sub>, IgG<sub>3</sub>, or IgG<sub>4</sub>; or  
the IgA is IgA<sub>1</sub> or IgA<sub>2</sub>.
- 20 64. The method of claim 38, wherein the agent is a small  
molecule.
65. The method of claim 38, wherein the agent  
specifically binds to CD40 on the cell surface.
- 25 66. The method of claim 65, wherein the agent is a  
protein.
67. The method of claim 66, wherein the protein is an  
antibody.
- 30 68. The method of claim 67, wherein the antibody is a  
monoclonal antibody.
69. The method of claim 68, wherein the monoclonal  
antibody is chimeric, humanized, or primatized.
- 35 70. The method of claim 66, wherein the protein  
comprises the extracellular region of CD40 ligand.
- 40 71. The method of claim 38, wherein the agent is

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5 nonprotein.

72. The method of claim 38, wherein the agent is selected from a library of known agents.

10 73. The method of claim 38, wherein the agent is modified from a known agent.

74. The method of claim 73 wherein the modified agent is designed by structure optimization of a lead inhibitory agent based on a three-dimensional structure of a complex of soluble extracellular region of CD40 ligand or portion thereof with the lead inhibitory agent.

20 75. The method of claim 38, wherein the agent is selected by a screening method, which comprises:

isolating a sample of cells;

25 culturing the sample under conditions permitting activation of CD40-bearing cells;

contacting the sample with cells expressing a protein which is specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 10916, or with a protein which is specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 10916, effective to activate the CD40-bearing cells;

30 contacting the sample with an amount of the agent effective to inhibit activation of the CD40-bearing cells if the agent is capable of inhibiting activation of the CD40-bearing cells; and

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- 5 determining whether the cells expressing the protein  
which is specifically recognized by monoclonal  
antibody 5c8 produced by the hybridoma having ATCC  
Accession No. HB 10916, or with the protein which is  
specifically recognized by monoclonal antibody 5c8  
10 produced by the hybridoma having ATCC Accession No.  
HB 10916, activate the CD40-bearing cells in the  
presence of the agent.
- 15 76. The method of claim 75, wherein the agent is  
selected from a library of known agents.
77. The method of claim 76, wherein the known agents are  
nonprotein agents.
- 20 78. A method of inhibiting an inflammatory response in  
a subject, comprising the method of claim 38.
79. A method of treating a condition dependent on CD40  
25 ligand-induced activation of fibroblast cells in a  
subject, comprising the method of claim 38.
80. The method of claim 79, wherein the fibroblasts are  
synovial membrane fibroblasts, dermal fibroblasts,  
30 pulmonary fibroblasts, or liver fibroblasts.
81. The method of claim 79, wherein the condition is  
selected from the group consisting of arthritis,  
scleroderma, and fibrosis.
- 35 82. The method of claim 81, wherein the arthritis is  
rheumatoid arthritis, non-rheumatoid inflammatory  
arthritis, arthritis associated with Lyme disease,  
or osteoarthritis.
- 40 83. The method of claim 81, wherein the fibrosis is

- 5 pulmonary fibrosis, hypersensitivity pulmonary  
fibrosis, or a pneumoconiosis.
- 10 84. The method of claim 83, wherein the pulmonary  
fibrosis is pulmonary fibrosis secondary to adult  
respiratory distress syndrome, drug-induced  
pulmonary fibrosis, idiopathic pulmonary fibrosis,  
or hypersensitivity pneumonitis.
- 15 85. The method of claim 83, wherein the pneumoconiosis  
is asbestosis, siliconosis, or Farmer's lung.
- 20 86. The method of claim 81, wherein the fibrosis is a  
fibrotic disease of the liver or lung.
- 25 87. The method of claim 86, wherein the fibrotic disease  
of the lung is caused by rheumatoid arthritis or  
scleroderma.
- 30 88. The method of claim 86, wherein the fibrotic disease  
of the liver is selected from the group consisting  
of:  
Hepatitis-C;  
Hepatitis-B;  
cirrhosis;  
cirrhosis of the liver secondary to a toxic  
insult;  
cirrhosis of the liver secondary to drugs;  
cirrhosis of the liver secondary to a viral  
infection; and  
35 cirrhosis of the liver secondary to an  
autoimmune disease.
- 40 89. The method of claim 88, wherein the toxic insult is  
alcohol consumption.
90. The method of claim 88, wherein the viral infection

- 5 is Hepatitis B, Hepatitis C, or hepatitis non-B non-C.
- 10 91. The method of claim 88, wherein the autoimmune disease is primary biliary cirrhosis, or Lupoid hepatitis.
- 15 92. A method of treating a condition dependent on CD40 ligand-induced activation of endothelial cells in a subject, comprising the method of claim 38.
- 20 93. The method of claim 92, wherein the condition is selected from the group consisting of atherosclerosis, reperfusion injury, allograft rejection, organ rejection, and chronic inflammatory autoimmune diseases.
- 25 94. The method of claim 93, wherein the atherosclerosis is accelerated atherosclerosis associated with organ transplantation.
- 30 95. The method of claim 93, wherein the chronic inflammatory autoimmune disease is vasculitis, rheumatoid arthritis, scleroderma, or multiple sclerosis.
- 35 96. A method of treating a condition dependent on CD40 ligand-induced activation of epithelial cells in a subject, comprising the method of claim 38.
- 40 97. The method of claim 96 wherein the epithelial cells are keratinocytes, and the condition is psoriasis.
98. A method of inhibiting activation by CD40 ligand of myeloma cells bearing CD40 on the cell surface, comprising contacting the cells with an agent capable of inhibiting interaction between CD40

99. A method of inhibiting activation by CD40 ligand of myeloma cells bearing CD40 on the cell surface, in a subject, comprising administering to the subject an agent capable of inhibiting interaction between CD40 ligand and the cells, in an amount effective to inhibit activation of the cells in the subject.

15 100. A method of treating a condition dependent on CD40 ligand-induced activation of myeloma cells in a subject, comprising the method of inhibiting activation by CD40 ligand of myeloma cells bearing CD40 on the cell surface of claim 99.

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101. The method of claim 100, wherein the condition is multiple myeloma.

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